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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/881,526	SNODGRASS, H. RALPH	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *7-9 and 32-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 10-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/1/01,12/18/02*, 4/12/02, 3/15/02, 2/23/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 14 June 2001, which claims benefit of US provisional application 60/211,606, filed 14 June 2000. Claims 1-41, as originally filed, are pending.

Election/Restrictions

Applicant's election with traverse of Group I and the chemical composition having predetermined toxicity that is a the hepatic toxin in the reply filed on 24 May 2004 is acknowledged. The traversal is on the ground(s) that it would not be unduly burdensome to search all of the restriction groups together. This is not found persuasive with respect to Groups I-IV because, as pointed out in the previous Office Action, each of the distinct Inventions comprise distinct elements and therefore cannot be searched coextensively. For example, a search of a method of creating a nucleic acid hybridization profile according to Group I would not encompass art directed to a method of creating a protein expression profile according to Groups II and III, and a search of the immunoassay of Group II would not encompass the mass spectrometry assay of Group III. Likewise, a search of an integrated system comprising an array reader according to Group IV would not encompass a method of creating a molecular profile according to Groups I-III and *vice versa*.

Applicant's arguments are persuasive with regard to restriction of the method to chemical compositions having a single predetermined toxicity. Thus, the elected method will be examined for all of the chemical compositions having predetermined toxicities recited in the claims.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-9 and 32-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 24 May 2004.

Claims 1-6 and 10-31 are presently under consideration.

Claim Objections

Claim 19 is objected to because of the following informalities: There should be a conjunction between "2" and "10-18" in line 2-3. Amending the claim to read "produced by a method according to any one of the claims 2 or 10-18" would be remedial. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 19 and 20 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to a library of molecular profiles wherein said profiles are defined in the fourth full paragraph on page 9 of the specification as "a pattern of alterations in gene or protein expression, or both, in LSCs contacted by [a] chemical composition compared to similar LSCs in contact only with culture medium."

Product claims may be directed to either machines, manufactures, or compositions of matter. A machine is "a concrete thing, consisting of parts or of certain devices and combinations

of devices." Burr v. Duryee, 68 U.S. (1 Wall.) 531, 570 (1863). A manufacture is "the production of articles for use from raw or prepared materials by giving to these materials new forms, qualities, properties or combinations, whether by hand labor or by machinery." Chakrabarty, 447 U.S. at 308, 206 USPQ at 196-97 (quoting American Fruit Growers, Inc. v. Brogdex Co., 283 U.S. 1, 11 (1931)). A composition of matter is "a composition of two or more substances [or] . . . a[] composite article, whether [it] be the result[] of chemical union, or of mechanical mixture, or whether . . . [it] be [a] gas[], fluid[], powder[], or solid[]." Id. at 308, 206 USPQ at 197 (quoting Shell Development Co. v. Watson, 149 F. Supp. 279, 280, 113 USPQ 265, 266 (D.D.C. 1957), aff 'd per curiam, 252 F.2d 861, 116 USPQ 428 (D.C. Cir. 1958)). The instant library is neither a machine, manufacture nor compositions of matter. It is in fact information, which is not patentable subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The claims are directed to a library of molecular profiles of chemical compositions having predetermined toxicities produced by contacting an isolated population of mammalian liver stem cells (LSCs) with a chemical composition having predetermined toxicities and recording alterations in gene expression in response to the chemical composition, and compiling a library by repeating the contacting and recording steps with multiple chemical compositions. Thus, the claims thus directed to a library comprised of LSC gene expression profiles obtained for any chemical composition having predetermined toxicity.

In the instant case, the claimed library is made up of an unlimited number of distinct species of expression profiles which are defined in the fourth full paragraph on page 9 of the specification as, "a pattern of alterations in gene or protein expression, or both, in LSCs contacted by the chemical composition compared to similar LSCs in contact only with culture medium." By way of illustration, the specification discloses a library of molecular profiles obtained for two unidentified compounds, wherein the profiles are comprised of mass spectrometry data for nuclear proteins, small nuclear proteins, small cytoplasmic proteins and large cytoplasmic proteins (see especially the discussion beginning at page 38, line 24 and continued through page 42, line 2 and Figures 1-4). However, it would seem that the molecular

profile for any given chemical composition is a unique property of that chemical composition, and a disclosure of a molecular profile for any one chemical composition is not representative of a molecular profile for any other chemical composition. Furthermore, given posttranscriptional regulation of protein expression, the skilled artisan would not expect a protein expression profile of a given chemical composition to be representative of a nucleic acid expression profile of that same compound. Thus, the library comprised of protein expression profiles for two compounds disclosed in the specification does not demonstrate possession of any library of molecular profiles other than the library actually reduced to practice.

Although the specification provides a description of how one might compile a library of molecular profiles, an adequate written description of a molecular profile requires more than a mere statement that it is part of the invention and reference to a potential method for producing it; what is required is a description of the molecular profile itself. It is not sufficient to define an invention solely by its principal property (*i.e.*, a pattern of alterations in gene or protein expression, or both, in LSCs contacted by the chemical composition compared to similar LSCs in contact only with culture medium) because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any such pattern of alterations in gene or protein expression. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all DNA's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived.

Claims 1-6 and 10-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The instant invention is directed to a method of compiling a library of molecular profiles of chemical compositions, a library of molecular profiles made by the method and a method of typing, ranking or assessing toxicity of a test chemical composition, wherein the methods comprise contacting an isolated population of mammalian liver stem cells (LSC) with said chemical compositions and recording alterations in gene expression. The chemical compositions of the claims are not limited to any particular type of composition, or, in dependent claims, limited to therapeutic agents, neurotoxins renal toxins hepatic toxins, toxins of hematopoietic cells, myotoxins, agents toxic to reproductive organs, teratogenic agents, carcinogens, agricultural chemicals, cosmetics and environmental contaminants. The specification teaches that the claimed methods can be used to assess toxicity

of chemical compositions by comparing expression patterns of LSCs exposed to new or previously untested agents to a library of profiles of expression induced by agents of known toxicity, such that predictions can be made as to the likely type of toxicity of the new agent (second paragraph on page 15). The specification asserts, "the outcome of such comparisons provides information for one to predict the likelihood of whether the test composition is toxic, what type of toxicities, and how toxic it would be as compared to other compositions" (first paragraph on page 37). It is also clear from teachings found throughout the specification that the invention is intended to be used to predict the toxic effects that would be manifest *in vivo*. As the enabling disclosure must teach the skilled artisan how to make and use the claimed invention, the specification must teach the skilled artisan how to make a library of molecular profiles of chemical compositions that can be used to predict the likelihood of whether a test composition is toxic, what type of toxicity, and how toxic it would be as compared to other compositions; and how to type, rank and assess toxicity of a test chemical composition using data obtained by contacting an isolated population of mammalian LSCs with the test chemical composition and comparing the molecular profile of the test chemical composition with a library of molecular profiles.

State of the prior art and level of predictability in the art: The relevant art teaches that establishing an *in vitro* model system having the capacity to predict the likelihood of toxicity, the type of toxicity, and/or the degree of toxicity is far from routine.

First, the art teaches that, before an *in vitro* system can be used to predict the *in vivo* toxicity of a compound, the model system must be validated. Davila *et al.* (1998) *Annu. Rev. Toxicol.* 38:63-96 (made of record in the IDS filed 23 February 2004), teaches that before *in*

vitro findings may be correlated with *in vivo* human toxicity, certain basic steps should be followed (page 64). These include: identify the appropriate target organ and species; develop and characterize a suitable *in vitro* system; with model test compounds and reasonable *in vitro* concentrations and exposure times, perform toxicity studies; employ a battery of cytotoxic assays to evaluate the compounds; after evaluation of the model compounds, measure the toxicity of unknown or previously untested agents; compare and contrast their toxicity with the model compounds; and examine mechanisms of toxicity with more detailed and in-depth investigations (Table 1). Davila teaches, "[a]fter thorough examination of the model compounds to demonstrate the validity and sensitivity of the *in vitro* system to detect known toxic compounds, unknown or untested compounds can be evaluated with the *in vitro* model system" (bridging pages 64-65). Thus, Davila teaches that careful experimentation is required to establish that the endpoint measured in the *in vitro* model system can be reliably correlated with a given *in vivo* toxicity before data obtained *in vitro* can be used to predict the toxic properties of a compound as they are manifest *in vivo*.

In an article published well after the effective filing date of the instant application, Waring *et al.* (2002) *Curr. Opin. Mol. Ther.* 4:229-235 (made of record in the IDS filed 23 February 2004) also questions the predictive value of *in vitro* systems, particularly with respect to toxicogenomic methods. Waring *et al.* flatly states, "[i]t is too early to determine if gene expression markers for toxicity can be extrapolated from cell culture to animal systems" and "[c]learly, a great deal of additional research will be required in order to consistently link the changes seen *in vivo* and *in vitro*" (page 233, left column, second full paragraph). These assertions are based, in part, on the observation that 15 well-characterized hepatotoxins grouped

together differently and gave very different expression profiles in isolated rat hepatocytes versus in-life-treated rats. Tugwood *et al.* (2003) *Biomarkers* 8:79-92 (made of record in the IDS filed 23 February 2004) also questions the predictive value of *in vitro* experiments and particularly emphasizes the dedifferentiation of primary isolates in culture as a confounding factor in correlating *in vitro* data to *in vivo* effects (see especially the first full paragraph on page 84). These findings call into question even the limited expectation that toxicogenomic data obtained with a cells isolated from a particular organ can predict similar effects in that same organ *in vivo*, let alone an expectation that toxicogenomic data obtained *in vitro* using a primitive cell type can be used to generally predict toxicity in the many varied cell types that make up an animal.

Waring *et al.* teaches that among the questions that remain to be addressed even in 2002 are: whether gene expression alone is enough to predict and/or identify a mechanism of toxicity; how great the an effect time points and concentrations will have on the overall expression profile; and the ability of microarray analysis to identify cell-specific toxicity (third full paragraph in the left column on page 233). Furthermore, Waring *et al.* characterizes the majority of toxicogenomics used for safety evaluation as of 2002 as exploratory and applied in a case-by-case fashion. As a whole, the teachings of Waring *et al.* and Tugwood *et al.* indicate that the validity of *in vitro* toxicogenomic models for toxicity is at least as unpredictable as other systems, and also requires careful empirical verification to establish the predictive capabilities of the model system as described by Davila *et al.*

With regard to using primary cultures of LSCs to predict the *in vivo* toxic effects of a wide range of compounds, the art is mostly silent. Carere *et al.* (2002) *Toxicol. Lett.* 127:153-160 (made of record in the IDS filed 23 February 2004) speculates that stem cells may provide a

source of specialized cell types and may allow the study of toxicant interferences with development and specialization processes (paragraph bridging the left and right columns on page 155), but characterizes the state of the art in 2002 as "not ready for standardization and routine use" (second full paragraph in the right column on page 155).

The art also teaches that the correlative value of any particular toxicogenomic method is also unpredictable. Thomas *et al.* (2003; *Toxicogenomics*, pp. 31-38. Editor(s): Inoue and Pennie. Springer-Verlag Tokyo: Tokyo, Japan; made of record in the IDS filed 23 February 2004) teaches, "just identifying the disrupted pathways and associated gene expression changes do not necessarily provide a method to predict similar toxic responses with other chemicals or across species. A big challenge for the emerging field of toxicogenomics will be to develop models and tools that use gene expression measurements to ultimately predict toxicity in untested chemicals and also determine whether a similar toxic response will occur in humans" (first paragraph on page 32). Thus, Thomas *et al.* teaches that developing models and tools that use gene expression measurements to ultimately predict toxicity in untested chemicals remained a challenge to be overcome as late as 2003, and therefore was clearly not routine when the instant application was filed.

Thomas *et al.* teaches that there are two important points concerning development of predictive toxicological models using gene expression: the information contained within the predictor variables and the selection of a diagnostic subset of genes (first full paragraph on page 34). Thomas *et al.* teaches, "the classification of a set of chemicals into a toxicological class or endpoint based on gene expression is difficult due to the variety of potential mechanisms that underlie the toxicity of these chemicals" and cites examples of compounds that arrive at the same

toxic endpoint by distinct pathways (page 34). Thomas further teaches that interpreting toxicogenomic data is also complicated by the fact that "multiple factors converge to ultimately influence the manifestation of toxicity and associated gene expression patterns" (paragraph bridging pages 34-35). Although Thomas *et al.* is referring to the *in vivo* system, it is reasonable to assume that because factors such as time, dose, route of administration, age and sex would not be accounted for in *in vitro* models, these factors would create even greater uncertainty in using findings obtained in an *in vitro* system to predict the likelihood of whether a test composition is toxic, what type of toxicity, and how toxic it would be as compared to other compositions.

Thus, the teachings from the art clearly establish that at the time of filing, and well after, the skilled artisan would not be able to predict the presence, type or degree of toxicity based on data obtained with an *in vitro* toxicogenomic model without first establishing a nexus between the model system and the relevant *in vivo* system. Furthermore, the art teaches that establishing the nexus between an *in vitro* toxicogenomic system and an *in vivo* system was far from routine at the time of filing. Therefore, the skilled artisan must rely on the teachings of the instant disclosure to set forth the manner and process of making a library of molecular profiles of chemical compositions that can be used to predict the likelihood of whether a test composition is toxic, what type of toxicity, and how toxic it would be as compared to other compositions; and how to type, rank and assess toxicity of a test chemical composition using data obtained by contacting an isolated population of mammalian LSCs with the test chemical composition and comparing the molecular profile of the test chemical composition with a library of molecular profiles. Furthermore, these teachings must be set forth in such clear, concise, and exact terms as to enable the skilled artisan to practice the invention without undue experimentation.

Amount of direction provided by the inventor and existence of working examples: With regard to working examples, the specification describes a process of making a library of molecular profiles wherein alterations in protein expression elicited in LSCs by two different test compositions are determined (see especially Figures 1-4 and the legends thereto). However, the specification is silent with regard to the predictive value of the data set presented and provides no evidence that the data can be used to establish the toxic properties of a test compound. Thus, the specification does not appear to contain a single working example of the invention such that it can be used to establish toxicity of a compound. Therefore, the question at hand is whether the specification provides sufficient teaching to enable the skilled artisan to extend the method reduced to practice such that it could be used for the purpose set forth in the specification without the need for undue experimentation.

On page 11, the specification asserts that the invention achieves the goals set forth in the specification by "exploiting the properties of pluripotent liver stem cells (LSCs)." Applicant speculates that, "[b]ecause of its pluripotency in differentiating into multiple tissue types, an isolated population of LSCs provides a much closer model to the complexity of *in vivo* systems than do traditional single cell or yeast assays" (second paragraph on page 11). However, this statement seems to be at odds with the teachings of Tugwood *et al.*, which suggest that dedifferentiation is damaging to the correlative value of an *in vitro* model system. Applicant's assertion seems to be based on a hypothesis that the relatively primitive nature of LSCs makes them more representative of the complex biology of an intact organism (see especially the discussion of the background art on pages 1-3 and the statement in the first paragraph on page 11), yet no data are presented to support this hypothesis. With regard to correlating the molecular

profiles with toxicities, the specification merely teaches that repeated iteration of the method of compiling a library of molecular profiles with "a reasonably large number" of chemical compounds of similar toxicity will provide patterns of gene or protein expression, or both, associated with that toxicity. However, this simple scheme for providing correlative data fails to account for the many variables that might confound obtaining a predictive data set, such as cell type specific effects, various pathways leading to common toxic outcomes, bioconversion of some compounds to toxic metabolites and various pharmacodynamic effects present in the *in vivo* system (e.g., sequestration or compartmentalization) that would not be accounted for in the *in vitro* system. Likewise, the teachings from the specification regarding how toxicities can by typed or ranked using the claimed method provide only that the molecular profile of test composition can be compared to that of a chemical composition or library of compositions with predetermined toxicities and the outcome of the comparison provides information for one to predict the likelihood of whether the test composition is toxic, what type of toxicities, and how toxic it would be as compared to the other known toxic compositions. However, these teachings are predicated on the assumption that expression profiles in LSCs are a viable model for toxicity *in vivo*, and that the system provides an accurate measure of toxicity regardless of the toxicant (i.e., to therapeutic agents, neurotoxins, renal toxins, hepatic toxins, toxins of hematopoietic cells, myotoxins, agents toxic to reproductive organs, teratogenic agents, carcinogens, agricultural chemicals, cosmetics and environmental contaminants) or organ system affected by the toxicity. Again, however, no data are provided to support this assumption. Thus, the specification stops well short of teaching the skilled artisan how the data obtained according to

the claimed method relate to the toxic properties of the test compounds as they are manifest *in vivo*.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Given the art recognized unpredictability of extrapolating *in vitro* toxicogenomic data to predict *in vivo* toxicity for any given type of toxicity or target organ, the skilled artisan would clearly have to engage in undue empirical experimentation to confirm that the claimed method could be used to predict any particular type of toxicity in any particular organ system, let alone the broad scope contemplated in the application. Davila *et al.* teaches that merely establishing that the claimed method could be used to predict a single type of toxicity to a single organ system would require developing and characterizing the *in vitro* MSC system as a model for the appropriate target organs; performing toxicity studies with model test compounds at reasonable *in vitro* concentrations and exposure times; employing a battery of cytotoxic assays to evaluate the compounds; after evaluation of the model compounds, measuring the toxicity of unknown or previously untested agents; comparing and contrasting their toxicity with the model compounds; and examining mechanisms of toxicity with more detailed and in-depth investigations.

The art published even well after the effective filing date of the in instant application teaches that "it is too early to determine if gene expression markers for toxicity can be extrapolated from cell culture to animal systems" and "[c]learly, a great deal of additional research will be required in order to consistently link the changes seen *in vivo* and *in vitro*" (*Id.*), and identifies developing models and tools that use gene expression measurements to ultimately predict toxicity in untested chemicals and also determine whether a similar toxic response will

occur in human as a big challenge for the emerging field of toxicogenomics (*Id.*). Clearly, therefore, the task of developing the instant claimed method such that it can be used to predict the likelihood of whether the test composition is toxic, what type of toxicities, and how toxic it would be as compared to the other known toxic compositions would require experimentation well beyond what is considered routine in the art. Therefore, claims 1-6 and 10-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M Sullivan, Ph.D.